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Major Article

SARS-CoV-2 positivity rates in asymptomatic workers at a cancer referral center in Mexico City: A prospective observational study in the context of adapting hospitals back to regular practice

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A B S T R A C T

Background: Healthcare workers are at increased risk of SARS-CoV-2 infection. The positivity rates in hospitals that do not receive patients with COVID-19, such as the National Cancer Institute (INCan) in Mexico, and the associated factors are unknown.

Objective: To assess the incidence and factors associated with SARS-CoV-2 infection in health workers at INCan.

Methods: A cohort study of 531 workers who were followed for 6 months. RT-PCR analysis of saliva and nasopharyngeal swab samples were used in the baseline and to confirm cases during follow-up The incidence rate ratio was calculated according to the measured characteristics and the associated factors were calculated using logistic regression models.

Results: Out of 531 workers, 9.6% tested positive for SARS-CoV-2, Being male (RR: 2.07, 95% CI: 1.1-3.8, $P = .02$), performing administrative tasks (RR: 1.99, 95% CI: 1.0-3.9, $P = .04$), and having relatives also working at INCan (RR: 3.7, 95% CI: 1.4-9.5, $P < .01$) were associated with higher positivity rates.

Discussion: Incidence of positive cases in health workers were similar to that reported in non-COVID hospitals from other countries.

Conclusions: Even though active surveillance helped to detect a significant number of asymptomatic infections, it is still necessary to reinforce preventive measures in non-medical staff to prevent nosocomial transmission.

INTRODUCTION

Mexico is one of many countries whose health care systems collapsed due to the COVID-19 pandemic.[1,2] Further, Mexican health care workers experienced the highest COVID-19 death rate worldwide (3.8%),[3] posing a serious challenge to health authorities attempting to prevent nosocomial transmission.

During this health care crisis, 33 secondary and tertiary public hospitals in Mexico were converted to treat COVID-19 patients. Meanwhile, other facilities, such as the National Cancer Institute (INCan in Spanish), continued to treat patients with cancer and were

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called “non-COVID hospitals”[4]; specifically, INCan set up an intensive care unit (ICU) for treatment of COVID-19 patients in an exclusive ward with eight intensive care beds and 18 additional beds. The present study aims to assess the incidence of infection with SARS-CoV-2, the virus that causes COVID-19, in health workers at INCan and their associated risk factors.

METHODS

A prospective open cohort study of health care workers at INCan was conducted between May and October 2020. All subjects gave their consent to participate. The present study was conducted in accordance with the Helsinki Declaration and approved by the INCan Research Ethics Committee (CEI/1479/20) (020/005/DII). The surveillance model followed the “Standard guideline for laboratory and epidemiological surveillance of COVID-19″ issued by the Secretariat of Health.[5]

Setting

INCan is a 133-bed teaching hospital for adolescents and adult patients with cancer, and it employs 2,922 individuals. During the study period, 165 (5.64%) health care workers were involved in frontline activities related to COVID, 2,122 were involved in non-COVID clinical wards or clinical duties (72.62%), and 635 (21.17%) were in administrative jobs with non-direct patient contact; 67% were women, and 33% were men, with a mean age of 45. During the pandemic, our institution suspended in-person academic and teaching activities, a respiratory triage area was installed for patients and workers, and the flow of patients was reduced. In addition, medical consultations, laboratory studies and office activities were rescheduled. All workers ≥ 65 or with comorbidities (diabetes mellitus, obesity, arterial hypertension, chronic lung disease or cancer) or those who were pregnant ceased work indefinitely to safeguard their health and prevent severe illness due to SARS-CoV-2 infection.

Study population and follow-up

Asymptomatic health care workers at INCan were invited to participate. We excluded subjects who had a history of symptoms consistent with COVID-19 and a positive rapid or RT-PCR test. Every two weeks, they were asked to fill out a questionnaire and give blood samples (to measure antibodies whose analysis is still under development), as well as saliva and nasopharyngeal swabs to confirm suspected cases. Workers who did not attend at least two consecutive follow-up visits were eliminated from the analysis.

Epidemiological surveillance questionnaire

During the baseline visit, participants completed an online questionnaire on SARS-CoV-2 exposure. The questionnaire included sociodemographic and clinical variables, as well as data representing higher levels of exposure. The questionnaire was then administered every 5 days for 6 months.

Definition of suspected and confirmed cases

The definitions of suspected and confirmed SARS-CoV-2 cases were adopted from the Secretary of Health in Mexico, as well as measures for epidemiological surveillance, disease prevention, health risk control, COVID-19 precautions, isolation definitions, contact studies and sampling procedures according to the epidemiological surveillance strategies of our country.[5] Suspicious cases were identified via the questionnaire throughout follow-up; in these cases, an RT-PCR test was performed on a saliva sample and in nasopharyngeal swab to confirm the case (an analysis of our group of researchers showed a concordance of 95.2% (kappa 0.852, P = .0001)).[6]

Sample collection and analysis

Nasopharyngeal swab and saliva samples were collected from all participants at the beginning of the study to detect SARS-CoV-2 through RT-PCR; subsequently, saliva samples and nasopharyngeal swabs were collected only in suspicious cases (by symptoms or contact with confirmed cases). A trained physician performed the sample collection with a flexible swab that was inserted into both nostrils until reaching the posterior nasopharynx of the patient, and it was then withdrawn after several seconds. The swabs were placed in 3 mL of sterile viral transport medium and deposited into a single viral transport tube.

The saliva sample collection was carried out using an Oragene collection tube, in which 5 mL of saliva from each patient was deposited without any stimulation; the patients were asked not to perform oral hygiene or rinse their mouths before sampling.

Both the saliva sample and the nasopharyngeal swab were processed for viral RNA extraction and RT-PCR for virus detection. The concordance between the saliva sample and the swab was analyzed. In case of disagreement, the result obtained through the nasopharyngeal swab was considered definitive.

Sample processing was performed by the National Institute of Genomic Medicine under the criteria established by the Institute for Epidemiological Diagnosis and Reference to manage molecular samples used to diagnose SARS-CoV-2 infection.

Both swab and saliva samples were processed in the Thermo Fisher MagMax viral RNA kit-based viral RNA purification system, and the RT-PCR test was carried out using the TaqMan 2019-nCoV Assay kit. version 1 (singleplex) on a Thermo Fisher QuantStudio 5 device.

Statistical analysis

Descriptive analysis included measures of central tendency and dispersion of sociodemographic and clinical characteristics depending on the type of variables and their distribution. We estimated the incidence rate (IR) of SARS-CoV-2 infection by dividing the number of new PCR-confirmed cases by the person-time at risk, and the incidence rate ratio (IRR) was calculated between exposure categories. We performed a logistic regression model using variables potentially associated with SARS-CoV-2 positivity rates based on their statistical significance and biological plausibility. The statistical analysis was performed using STATA v.14.

RESULTS

Of the 544 workers who agreed to participate, 13 participants were eliminated, 2 withdrew consent, and 11 were lost to follow-up (they did not attend at least two follow-up visits), leaving a final sample of 531 workers who underwent a total of 1,278 RT-PCR tests and nasopharyngeal swabs Figure 1.

The mean age of the 531 health workers assessed was 40.5±11.3 years; 72.3% were women, 27.6% were men, and 9.6% tested positive for SARS-CoV-2 during the study.

Of all participants, 68% were health care professionals having direct contact with patients, 59.7% commuted to work by car, 60% lived with fewer than 3 people, and 55% had contact with at least one confirmed positive case. The workplace was referred to as the source of contact by 90.3% of those who had contact with at least 1 confirmed positive case. Most participants wore masks at work (97.2%) and reported to perform daily activities out of the office and home

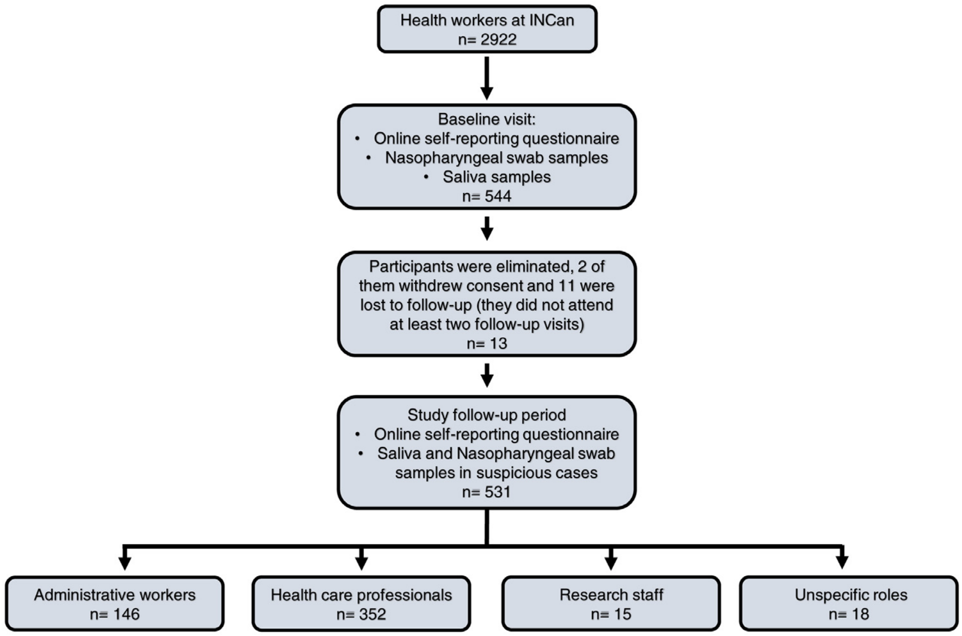

Fig 1. Study population.

within the past month (64.9%). A significant number of workers had relatives also working at INCan (26.5%).

Obesity was the most common comorbidity (26.1%), followed by hypertension (8.6%) and diabetes (4.9%).

Two factors were protectors against SARS-CoV-2 infection: having contact with a positive case in the workplace (IRR: 0.3, 95% CI: 0.15-0.99, $P = .01$) and wearing a mask when performing tasks (IRR: 0.19, 95% CI: 0.06-0.73, $P = .01$).

The clinical, sociodemographic and risk data for SARS-CoV-2 of the subjects included in this study are provided in Table 1.

The most common symptoms in the 51 health workers who tested positive for SARS-CoV-2 were fever (84.3%), headaches (49%), myalgia (41.1%), cough and odynophagia (35.2%). Asymptomatic cases accounted for 41.1% of positive cases. The risk of testing positive increased when participants reported having 1 - 3 symptoms (IRR: 2.1, 95% CI: 1.1-4.0, $P < .01$). Table 2

Multivariate analysis

The following variables were significantly associated with a higher likelihood of SARS-CoV-2 infection: being male (OR: 2.07, 95% CI 1.11-3.86), performing administrative duties (OR: 1.99, 95% CI 1.00-3.96), and having relatives also employed at INCan (OR: 3.76, 95% CI 1.47-9.57). All of these variables adjusted by living with more than 3 people and contact with a positive case are shown in Table 3.

DISCUSSION

Our study revealed a SARS-CoV-2 positivity rate of 9.6%. Men were at a higher risk of infection despite the smaller proportion of men in the sample. Administrative staff and employees who had relatives also working at INCan were among the infected. These findings agree with those of Lombardi et al., who identified a positivity rate of 8.8%. However, in their study, physicians had the highest number of positive tests.[7] Algado-Sellés et al. reported a COVID-19 prevalence of 4% (95% CI: 3.4-4.6) in Spanish health workers,[8] but they only assessed symptomatic cases; however, they considered that the prevalence would be 4.7%-5-3% if they included asymptomatic cases. The aforementioned authors stated that positivity rates were higher due to exposure to patients. Our study found that nonmedical staff at INCan had a higher risk of testing positive for SARS-CoV-2 (RR: 1.99, 95% CI: 1.0-3.96, $P = .04$) than medical staff.

Furthermore, regular follow-up using RT-PCR tests allowed us to determine the incidence of the disease and to identify 41% of asymptomatic cases that could have gone unnoticed.

Kim R. et al. suggested that health care workers developed a milder form of the disease in comparison with the general population,[9] which could be true in our sample due to widespread mask-wearing, a younger mean age, and fewer comorbidities.

Our study revealed that being male was associated with a higher risk of SARS-CoV-2 positivity (RR: 2.07, 95% CI, $P = .02$), which is consistent with sociocultural and biological factors related to molecular and cell markers that make men susceptible to infection, severe disease, and higher mortality.[10,11] The number of women in our study was higher than that of men, so we do not consider that the observed differences are due to working conditions that increase men's exposure to the virus.

We demonstrated the risk of infection when employees had relatives working in the same hospital. In a systematic review, Fung et al. revealed that households are a main source of infection.[12] We could speculate that a worker's individual risk adds to the risk of another relative working in the health sector. Some employees, mostly nurses and technicians, often work in other hospitals on different shifts.

Our study has some limitations. First, health-care workers with low and medium exposure risk at INCan took on riskier tasks during the pandemic due to the surging demand for care services and operational needs. Hence, we cannot accurately estimate the levels of exposure. Additionally, workers might not be aware of their exposure. For instance, Jiang L observed that administrative staff might have less contact with patients, but their contacts are of longer duration than those of the medical staff.[13] Examining the positive cases in health care workers, as well as their roles and workplaces, could help reduce unnecessary interactions among the staff and prevent transmission.

Liang En et al. proposed an approach based on individual responsibility and surveillance of nosocomial transmission in nonclinical

Table 1
Association between occupational and clinical variables in 531 health workers at INCan who underwent nasopharyngeal swabbing to detect SARS-CoV-2 infection

	Workers n	(%)	Incidence Rate Ratio	95% CI	*P* value*
Age					
<30	103	19.43	Reference		
30-39	152	28.68	1.39	0.63-3.32	.38
40-49	143	26.98	0.76	0.30-1.97	.53
50-59	108	20.38	0.60	0.19-1.76	.31
>60	24	4.53	0.38	0.00-2.71	.38
Sex					
Women	384	72.3	Reference		
Men	147	27.6	1.7	0.91-3.10	.07
Occupation					
Administrative workers	146	28.4	Reference		
Health care professionals	352	68.6	0.67	0.37-1.26	.18
Research staff	15	2.92	0.55	0.01-3.44	.63
Type of transportation to work					
Private car or other	310	59.7	Reference		
Public transportation	210	40.3	0.95	0.49-1.79	.88
Number of people living in the household					
Three or fewer	323	60.8	Reference		
More than 3	208	39.1	1.69	0.94-3.06	.06
Contact with a positive case					
No	147	27.51	Reference		
Yes	290	55.03	1.78	0.83-4.24	.06
Does not know	92	17.46	1.66	0.60-4.62	.13
Source of contact with positive cases					
Other	28	9.66	Reference		
Workplace	262	90.34	0.36	0.15-0.99	.01*
Wearing mask at work	489	97.22	0.19	0.06-0.73	.01*
Relative also working at INCan	133	26.5	2.36	0.82-5.55	.07
Going out (Grocery, medicine, or health services)	342	64.9	0.86	0.47-1.62	.62
Family gatherings during the last month	45	8.5	1.13	0.35-2.84	.75
Diabetes	26	4.9	0.35	0.00-2.08	.3
Asthma	20	3.7	1.12	0.13-4.29	.8
Hypertension	46	8.6	1.23	0.43-2.90	.6
Obesity	139	26.1	1.05	0.53-1.97	.84
Smoking	43	8.1	1.26	0.39-3.16	.59
Dyslipidemia	25	4.7	0.37	0.00-2.20	.33
Taking any medication	174	32.9	0.82	0.42-1.53	.53

Note: Missing values indicate missing or unspecified information in the online self-reporting questionnaire.
**P* value ≤ .05.

areas.[14] Training should be provided to health workers whose job descriptions make them less familiar with infection prevention protocols, especially after collecting evidence on the impact of case detection and the use of personal protective equipment to reduce transmission.[15]

The present study drew on the experience of one of the most important hospitals not focused on COVID in Mexico. Our findings will be useful in improving protocols and meeting future challenges posed by this pandemic, especially in the context of cancer treatment in hospitals

Table 2
Association between symptoms and positive tests among 51 workers tested for SARS-CoV-2 at INCan

	Workers n =51	(%)	Incidence Rate Ratio	95% CI	*P* value*
Fever	43	84.3	1.28	0.52-2.76	.50
Cough	18	35.2	1.30	0.69-2.38	.36
Odynofagia	18	35.2	1.15	0.61-2.11	.60
Chest pain	6	11.7	0.97	0.33-2.28	.99
Dyspnea	6	12	0.88	0.30-2.09	.82
Headache	25	49	0.98	0.54-1.77	.95
Myalgia	21	41.18	1.16	0.63-2.10	.59
Arthralgia	13	25.4	1.17	0.57-2.26	.59
Coryza	11	21.57	1.57	0.72-3.11	.19
Conjunctivitis	4	7.8	0.68	0.18-1.88	.50
Anosmia	4	7.8	0.76	0.20-2.09	.65
Diarrhea	9	17.65	0.89	0.38-1.85	.78
Number of symptoms					
None	21	41.18			
1-3	27	52.94	2.15	1.17-4.01	<.01*
4-5	2	3.92	0.96	0.10-3.95	1.03
More than 6	1	1.96	1.04	0.25-6.49	0.87

**P* value ≤ .05.

TRANSPARENCY STATEMENT

As the corresponding author of this paper, I, Nancy Reynoso Noverón, ensure on behalf of all authors and myself the data accuracy, integrity, and transparency; no relevant data have been omitted; any disagreement between authors was resolved and described.

Table 3
Multivariate logistic regression analysis of the risk of SARS-CoV-2 infection

	Odds Ratio	95% CI	*P* value*
Sex		Reference	
Women			
Men	2.07	1.11-3.86	0.02*
Occupation			
Health care professionals		Reference	
Administrative workers	1.99	1.00-3.96	0.04*
Research staff	0.89	0.11-6.73	0.91
Living with more than 3 people	1.78	0.98-3.24	0.05
Relatives also working at INCan	3.76	1.47-9.57	<0.01*
Contact with a positive case			
No		Reference	
Yes	1.75	0.75-4.07	0.19
Do not know if they had contact	2.05	0.80-5.24	0.13

**P* value ≤ .05.

REGISTRATION

The study was approved by the Research Committee and Research Ethics Committee of the National Cancer Institute (020/005/DII) (CEI/1479/20).

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References

1. Lal A, Erondu NA, Heymann DL, Gitahi G, Yates R. Fragmented health systems in COVID-19: rectifying the misalignment between global health security and universal health coverage. *Lancet*. 2021;397:61–67.
2. Instituto Nacional de Salud Pública. Tablero interactivo sobre COVID-19. 2021.
3. Agren D. Understanding Mexican health worker COVID-19 deaths. *Lancet*. 2020;396:807.
4. Gobierno de México. Secretaría de Salud. Lineamientos de Reconversión Hospitalaria. 2020.
5. Secretaría de Salud. Lineamiento estandarizado para la vigilancia epidemiológica y por laboratorio de la enfermedad respiratoria viral. 2021.
6. Herrera LA, Hidalgo-Miranda A, Reynoso-Noverón N, Meneses-García AA, Mendoza-Vargas A, Reyes-Grajeda JP. Saliva is a reliable and accessible source for the detection of SARS-CoV-2. *Int J Infect Dis*. 2021;105:83–90.
7. Lombardi A, Consonni D, Carugno M, et al. Characteristics of 1573 healthcare workers who underwent nasopharyngeal swab testing for SARS-CoV-2 in Milan, Lombardy, Italy. *Clin Microbiol Infect*. 2020;26. 1413.e9-1413.e13.
8. Algaldo-Sellés N, Gras-Valentí P, Chico-Sánchez P, et al. Frequency, associated risk factors, and characteristics of COVID-19 among healthcare personnel in a Spanish Health Department. *Am J Prev Med*. 2020;59:e221–e229.
9. Kim R, Nachman S, Fernandes R, et al. Comparison of COVID-19 infections among healthcare workers and non-healthcare workers. *PLoS One*. 2020;15:e0241956.
10. Jin JM, Bai P, He W, et al. Gender differences in patients with COVID-19: focus on severity and mortality. *Front Public Health*. 2020;8:152.
11. Haitao T, Vermunt JV, Abeykoon J, et al. COVID-19 and sex differences: mechanisms and biomarkers. *Mayo Clin Proc*. 2020;95:2189–2203.
12. Fung HF, Martinez L, Alarid-Escudero F, et al. The household secondary attack rate of SARS-CoV-2: A rapid review. *Clin Infect Dis*. 2020. :ciaa1558.
13. Jiang L, Ng HL, Ho HJ, Leo YS, Prem K, Cook AR. Contacts of healthcare workers, patients and visitors in general wards in Singapore. *Epidemiol Infect*. 2017;145:3085–3095.
14. En L, Mph W, Ying X, Sim J, Philip E, Nursing C, et al. Containment of COVID-19 cases among healthcare workers : the role of surveillance, early detection, and outbreak management. *Infect Control Hosp Epidemiol*. 2020;41:765–771.
15. El Bushra HE, Al Arbash HA, Mohammed M, et al. Outcome of strict implementation of infection prevention control measures during an outbreak of Middle East respiratory syndrome. *Am J Infect Control*. 2017;45:502–507.